REMARKS

Claims 1, 3, 5, 6, 8, 12, 13, 15-18, 20-23, 31, 32, 34-37 and 50 are pending in the present application. Claim 3 is canceled herein without prejudice to Applicant's right to pursue the subject matter of this claim in a related application. Claims 1, 18, 31, 34 and 50 are amended herein to specify that certain recited cells are $CD34^-$, $OCT\text{-}4^+$ and $SSEA3^-$. Support for these amendments is found in the published application at least at paragraphs [0012] and [0022]. No new matter is added by these amendments. New claims 54-57 are added. Support for new claims 54-57 is found in the published application at least at paragraphs [0012] and [0022]. Upon entry of this response, claims 1, 3, 5, 6, 8, 12, 13, 15-18, 20-23, 31, 32, 34-37, 50 and 54-57 will be pending in the application.

The Rejection Under 35 U.S.C. § 112, First Paragraph Should Be Withdrawn

Claims 1, 3, 5, 6, 8, 12, 13, 15-18, 20-23, 31, 32, 34-37 and 50 remain rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient written description and constituting new matter. *See* Office Action at pages 3-6. Without conceding the propriety of the rejection, and solely to facilitate allowance of the claims, claims 1, 18, 31, 34 and 50, from which the remaining claims ultimately depend, have been amended to specify that the recited cytotherapeutic units comprise cells that are $CD34^-$, $OCT\text{-}4^+$ and $SSEA3^-$.

The rejection maintains the contention that the disclosure does not sufficiently describe a cytotherapeutic unit comprising a plurality of cells that are $CD34^+$ and cells that are $CD34^-$ and $OCT\text{-}4^+$. Respectfully, the rejection provides no basis for the contention that "[t]he skilled artisan would not envision a population of potent cells specifically isolated from postpartum placental perfusate that are $CD34^-OCT\text{-}4^+$ cells from the instant disclosure that provides a list of possible antigenic markers." Office Action at page 5. As a result, the rejection does not establish that the subject matter of the amended claims is new matter. "The Examiner has the initial burden of presenting *evidence* or *reasoning* to explain why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims." Manual of Patent Examining Procedure, Eighth Edition Incorporating Revision No. 6, § 2163.04, page 2100-187, citing *In re Wertheim*, 541 F.2d 257, 263 (C.C.P.A. 1976); *see also Ex parte Sorenson*, 3 U.S.P.Q.2d 1462, 1463 (B.P.A.I. 1987).

The written description requirement is satisfied where the application "clearly convey[s] the information that an applicant has invented the subject matter which is claimed" and "put[s] the public in possession of what the applicant claims as the invention." Manual of Patent Examining Procedure (MPEP), Eighth Edition Incorporating Revision No. 5, § 2163, at page

2100-165 (citing *In re Barker*, C559 F.2d 588, 592 n.4 (C.C.P.A. 1977) and *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998). In fact, all aspects of the claimed cytotherapeutic units are described, *explicitly*, in the specification as detailed below.

The Specification Teaches That Cytotherapeutic Units Can Have Two Types of Potent Cells

The specification teaches that a cytotherapeutic unit can comprise more than one type of potent cell at least at paragraphs [0040] and [0043], and Example 2 of the published application.

The Specification Teaches That Cytotherapeutic Units Can Comprise CD34$^+$ Cells

The specification teaches cytotherapeutic units that comprise CD34$^+$ cells at least at paragraph [0040] of the published application, Example 1, Example 2, and Example 3. Moreover, it is apparent that the application teaches cytotherapeutic units comprising more than one type of cell, where at least one type is a CD34$^+$ cell, at paragraphs [0040] and Example 2.

The Specification Teaches That Cytotherapeutic Units Can Comprise CD34$^-$, OCT-4$^+$ Cells, and Cells That Are CD34$^-$, OCT-4$^+$ and SSEA3–

The specification teaches that cytotherapeutic units can comprise cells that "may be characterized by the presence of one or more of the following cell surface markers: CD10$^+$, CD29$^+$, **CD34$^-$**, CD38$^-$, CD44$^+$, CD45$^-$, CD54$^+$, CD90$^+$, SH2$^+$, SH3$^+$, SH4$^+$, **SSEA3$^-$**, SSEA4$^-$, **OCT-4$^+$**, and ABC-p$^+$." (Emphasis added.) *See* published application at least at paragraphs [0012] and [0022]. The cells described by the language "one or more of," in this instance, include cells that are CD34$^-$ OCT-4$^+$. Thus, the specification explicitly teaches cytotherapeutic units comprising cells that are CD34$^-$ and OCT-4$^+$. In the same manner, the specification explicitly describes cells that are CD34$^-$, OCT-4$^+$ and SSEA3$^-$. Clearly, the specification teaches cells having each of these markers. Moreover, the language "one or more of" includes "all." In other words, in one embodiment, the specification teaches that cytotherapeutic units can comprise cells that are *each of* CD10$^+$, CD29$^+$, **CD34$^-$**, CD38$^-$, CD44$^+$, CD45$^-$, CD54$^+$, CD90$^+$, SH2$^+$, SH3$^+$, SH4$^+$, **SSEA3$^-$**, SSEA4$^-$, **OCT-4$^+$**, and ABC-p$^+$. However, such cells need not be identified by *all* of these markers. Such cells can be identified as CD34$^-$ and OCT-4$^+$, or CD34$^-$, OCT-4$^+$ and SSEA3$^-$, and still be the same cell. For example, CD34$^+$ cells display many other markers besides CD34, yet are referred to as CD34$^+$ cells.

The Specification Teaches That Cytotherapeutic Units Can Comprise Cells From Placental Perfusate

The specification teaches that cytotherapeutic units can comprise cells from placental perfusate at least at paragraph [0013], which states that cells from perfusate are preferred, and paragraph [0043], and originally-filed claims 9 and 43. Moreover, the application teaches at least at paragraph [0043] that cytotherapeutic units can comprise more than one type of cell, at least one of which is obtained from placental perfusate.

Thus, the specification clearly teaches cytotherapeutic units comprising $CD34^+$ cells and $CD34^-$ $OCT\text{-}4^+$ cells, *e.g.*, $CD34^-$ $OCT\text{-}4^+$ $SSEA3^-$ cells, wherein the latter cells are obtained from placental perfusate. As such, the claimed invention is clearly described in the specification, and the claims comprise no new matter.

The rejection, after reviewing Applicant's explanation of support for the claims in the specification, contends that "the paragraphs provided by the Applicants are broad disclosures of a cytotherapeutic unit comprising at least some potent cells exhibiting CD34, CD8, CD10, OCT4, CD38, CXCR4, or CD117 . . ." Office Action at pages 4-5. This contention is, respectfully, inaccurate, because it focuses only on the teaching of paragraph [0011] of the specification. Examination requires a review of the *whole* application to determine how Applicant provides support for the claimed invention. *See* Manual of Patent Examining Procedure, Eighth Edition Incorporating Revision No. 5 ("M.P.E.P.") § 2163(II)(*A*)(2), pages 2100-177 to 2100-178.

The rejection contends that the specification does not disclose the exact embodiment of a cytotherapeutic unit comprising $CD34^+$ cells "and the specific combination of $CD34^-$ $OCT\text{-}4^+$ cells isolated from postpartum placenta perfusate." Office Action at page 5. The specification is not required to disclose every embodiment of an invention *in haec verba* in order to satisfy the written description requirement. *See* M.P.E.P. § 2163.03 at page 2100-175, left column. Nor is the specification required to exemplify the recited embodiment. "As explained by the Federal Circuit, '(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met . . . even where actual reduction to practice of an invention is absent . . .'" M.P.E.P. at § 2163, page 2100-179, citing *Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006); *see also LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005) (no examples necessary for written description); *Capon v. Eshhar*, 418 F.3d 1349, 1358 (Fed. Cir. 2005) ("The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the

claimed chimeric genes," wherein the genes were novel combinations of known DNA segments.). As explained by the Supreme Court in a different context, "[a] person of ordinary skill is also a person of ordinary creativity, not an automaton." *KSR International Co. v. Teleflex Inc.* 127 S. Ct. 1727, 1741 (2007). That is, a person of skill in the art, reading the present specification, would readily be able to tie together the disclosures as stated above to appreciate that Applicant had, in fact, invented the claimed cytotherapeutic unit.

The rejection characterizes Applicant's citation, in the Amendment filed November 14, 2007, of International Patent application Publication Nos. WO 02/064755 and WO 02/46373 as an improper incorporation by reference of "essential material," that is, a cytotherapeutic unit comprising $CD34^-$ $OCT\text{-}4^+$ cells obtained from placental perfusate. Office Action at page 5. However, as explained in detail above, the application describes cytotherapeutic units comprising $CD34^-$ $OCT\text{-}4^+$ cells, *e.g.*, $CD34^-$ $OCT\text{-}4^+$ $SSEA3^-$ cells, obtained from placental perfusate, in satisfaction of 35 U.S.C. § 112, first paragraph without any incorporation by reference.

Thus, the specification of the present application describes the claimed cytotherapeutic units in accordance with 35 U.S.C. § 112, first paragraph. Applicant respectfully requests that this rejection of the claims be withdrawn.

The Rejections Under 35 U.S.C. § 103 Should be Withdrawn

The Examiner has rejected the claims under 35 U.S.C. § 103(a) as obvious over several combinations of references. Applicant addresses each in turn below.

A determination of obviousness requires analysis of "1) 'the scope and content of the prior art'; 2) the 'differences between the prior art and the claims'; 3) 'the level of ordinary skill in the pertinent art'; and 4) 'objective evidence of nonobviousness'." *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1734 (2007) (quoting *Graham v. John Deere & Co. of Kansas City*, 86 S. Ct. 684 (1966)). In rejecting a claim for obviousness, an Examiner "must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art." "Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co.* v. *Teleflex Inc.*," 72 Fed. Reg. 57526, 57528 (2007) ("Guidelines"); *see also* Manual of Patent Examining Procedure, Eighth Edition Incorporating Revision No. 6, § 2100 at page 2100-118. The Examiner must consider the whole of art references, including parts that teach away from the claimed invention. MPEP § 2141.03(IV) at page 2100-126, citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (1984).

The Rejection Over Fasouliotis and Hwang

Claims 1, 3, 5, 6, 8, 15-18, 20-23, 31, 32, 34, 36, 37 and 50 are newly-rejected as obvious over Fasouliotis *et al.*, *Eur. J. Obstet. Gynecol. Reprod. Biol.* 90:13-25 (2000) ("Fasouliotis") in view of Hwang, U.S. Patent Application Publication No. 2004/0018617 ("Hwang").

As noted above, without conceding the propriety of the rejection, and solely to facilitate allowance of the claims, Applicant has amended claims 1, 18, 31, 34, and 51, from which all remaining rejected claims ultimately depend, to specify that the recited cytotherapeutic units comprise cells from placental perfusate that are $CD34^-$, $OCT\text{-}4^+$ *and* $SSEA3^-$. Fasouliotis does not teach or suggest $CD34^-$, $OCT\text{-}4^+$ cells isolated from placental perfusate, as acknowledged on page 9 of the Office Action, and, as such, does not teach or suggest cells that are $CD34^-$, $OCT\text{-}4^+$ *and* $SSEA3^-$.

The rejection cites Hwang as teaching cells that are $CD34^-$ and $OCT\text{-}4^+$; however, Hwang does not teach or suggest cells that are $CD34^-$, $OCT\text{-}4^+$ and $SSEA3^-$. Instead, Hwang ostensibly discloses pluripotent cells that are $SSEA3^+$. *See*, *e.g.*, Hwang at Example 4, which discloses only $SSEA3^+$ cells; *see also* paragraph [0012] (indicating that the cells can be identified as $SSEA3^+$). It is important to note that cells expressing SSEA3 is not *one* embodiment of the pluripotent cells disclosed in Hwang, but is the *only* embodiment, because Hwang teaches, without reservation, that the claimed cells "have phenotypes characteristic of undifferentiated ES cells." Hwang at paragraph [0010]; *see also* Example 4. It is known that human embryonic stem cells are $SSEA3^+$. *See*, *e.g.*, Thomson, *Science* 282:1145-1147 (1998), cited in Hwang at paragraph [0010], a copy of which is attached hereto. Therefore, Hwang does not teach or suggest an embodiment in which the pluripotent cells are $SSEA3^-$. As such, the combination of Hwang and Fasouliotis fails to teach or suggest cells that are $CD34^-$, $OCT\text{-}4^+$ and $SSEA3^-$, and fails to teach or suggest all limitations of the claims as amended.

In fact, the combination of Fasouliotis and Hwang teaches away from the claimed cytotherapeutic units, because the references would lead one of ordinary skill in the art to produce cytotherapeutic units using cells that are, *inter alia*, $SSEA3^+$ rather than $SSEA3^-$. To combine the two references according to the rejection, a person of ordinary skill in the art would obtain cells by the method allegedly disclosed in Fasouliotis, and would culture those cells by the method of Hwang to produce pluripotent cells. However, those pluripotent cells would be $CD34^-$, $OCT\text{-}4^+$, and $SSEA3^+$, not $SSEA3^-$, as required by the present claims. As such, a person of ordinary skill in the art would not be motivated to combine the cited

references to produce the claimed cytotherapeutic units because there would be no reasonable expectation of success in doing so.

Moreover, the rejection does not make out a *prima* facie case of obviousness on other grounds. For example, the rejection contends that it would be obvious to isolate cells by the method of Fasouliotis, to culture such cells by the method of Hwang, and to "include them in the plurality of potent cells for a cytotherapeutic unit . . ." Office Action at page 10. The rejection also contends that "the samples taught by Fasouliotis et al would comprise at least about one hundred $CD34^+$ cells and meets the limitation of a cytotherapeutic unit comprising at least about one hundred $CD34^+$ cells." Office Action at page 9. However if cells collected according to Fasouliotis are used to generate the pluripotent cells of Hwang, $CD34^+$ cells are not retained. As such, a person of skill in the art would not be motivated by the combination of Hwang and Fasouliotis to produce the claimed cytotherapeutic unit, which comprises *both* $CD34^+$ cells and $CD34^-$, $OCT\text{-}4^+$ cells.

This contention also appears to confuse the *somatic cells* disclosed in Hwang, which are not the $CD34^-$, $OCT\text{-}4^+$ pluripotent cells, with the pluripotent cells themselves. For example, the rejection contends that "at least one of the somatic cells taught by Hwang would be isolated by using the method of Fasouliotis et al to isolate cells from umbilical cord blood, postpartum placenta and postpartum placenta perfusate." Office Action at page 10; *see also* page 10, line 21 to page 11, line 3. However, according to Hwang, somatic cells must be cultured by a specific method in order to produce the $CD34^-$, $OCT\text{-}4^+$ pluripotent cells. *See, e.g.*, paragraphs [009]-[0012] and Examples 2 and 3. As such, the $CD34^-$, $OCT\text{-}4^+$ pluripotent cells on which the rejection relies are not "isolated by the method of Fasouliotis," as the rejection contends, Office Action at page 11, and are not isolatable by such method.

Additionally, the Examiner contends, *inter alia*, that Hwang "teaches somatic stem cells that can be cultured to a phenotype resembling a pluripotent embryonic stem cell," wherein the cells "can be isolated from . . . placenta." Office Action at page 9. Applicants note that the pluripotent cells described in Hwang are not "isolated from" placenta. Instead, the pluripotent cells of Hwang are produced by obtaining cells from tissues and *then* culturing the cells under specific conditions. *See, e.g.*, Hwang at paragraph [0012]. Thus, the pluripotent cells described in Hwang are not "obtained from postpartum placental perfusate" as required by the claims any more than, for example, computer chips are "obtained from" silicon wafers. As such, a construction of the pending claims to include the cells of Hwang is unreasonable. *See In re American Academy of Science Tech Center*, 367 F.3d 1359, 1369 (Fed. Cir. 2004) (claims must be interpreted as broadly as their terms *reasonably* allow); *see also Chef America, Inc. v.*

Lamb-Weston, Inc., 358 F.3d 1371, 1372 (Fed. Cir. 2004) ("ordinary, simple English words whose meaning is clear and unquestionable, absent any indication that their use in a particular context changes their meaning, are construed to mean exactly what they say"); MPEP § 2111.01, page 2100-38. For this additional reason, the combination of Fasouliotis and Hwang does not teach or suggest the claimed cytotherapeutic units comprising $CD34^-$, $OCT\text{-}4^+$ and $SSEA3^-$ obtained from placental stem cells, and a person of ordinary skill would therefore not combine these two references to produce the claimed cytotherapeutic units.

Therefore, for the reasons provided above, the claims as amended are not obvious over the combination of Hwang and Fasouliotis because a person of ordinary skill in the art would not be motivated to combine, and would have no reasonable expectation of success in combining, these references to produce the claimed cytotherapeutic units. Applicant respectfully requests withdrawal of this rejection of the claims.

The Rejection Over Fasouliotis, Hwang and Ende

Claims 12 and 13 are rejected as obvious over Fasouliotis in view of Hwang, U.S. Patent Application Publication No. 2004/0018617 ("Hwang") and further tin view of Ende, *Life Sciences* 69(13):1531-1539 (2001). Office Action at pages 15-17.

The rejection cites Fasouliotis and Hwang for the same subject matter as in the rejection above. The Examiner cites Ende as additionally disclosing pooling of umbilical cord blood samples. Office Action at page 16.

As explained above, the combination of Fasouliotis and Hwang fails to render the claimed cytotherapeutic units obvious, because the combination of references not only fails to teach or suggest all of the recited limitations of the pending claims, but in fact teaches away from the claimed cytotherapeutic units, which comprise $CD34^-$, $OCT\text{-}4^+$, $SSEA3^-$ cells obtained from placental perfusate. Ende does not supply the missing subject matter lacking in the combination of Fasouliotis and Hwang, because Ende fails to teach or suggest $CD34^-$, $OCT\text{-}4^+$, $SSEA3^-$ placental cells obtained from placental perfusate. Moreover, even in view of Ende, Fasouliotis and Hwang still teach away from the claimed cytotherapeutic units. As such, a person of ordinary skill in the art, given Fasouliotis, Hwang and Ende, would not be able to produce the claimed cytotherapeutic units, and would have no motivation to do so. The claims as amended are therefore not obvious over the combination of Fasouliotis, Hwang and Ende.

For the above reasons, Applicant respectfully requests withdrawal of this rejection of the claims.

The Rejection Over Pykett, Fasouliotis and Hwang

Claims 1, 3, 5, 6, 8, 15-18, 20-23, 34-37 and 50 are rejected as obvious over Pykett, U.S. Patent No. 6,548,299 in view of Fasouliotis and Hwang. Office Action at pages 17-24. Applicant traverses as follows.

The rejection contends, *inter alia*, that Pykett discloses "a population of cells obtained from blood products comprising hematopoietic cells, including $CD34^+$ cells." Office Action at page 18. The rejection cites Fasouliotis and Hwang for the subject matter discussed above. The Examiner contends that it would be obvious to a person of ordinary skill in the art to produce ES like cells, as taught by Hwang, from the cells disclosed in Fasouliotis.

As noted above, without conceding the propriety of the Examiner's rejection, and solely to facilitate allowance of the claims, Applicant has amended claims 1, 18, 31, 34, and 51, from which all remaining rejected claims ultimately depend, to specify that the recited cytotherapeutic units comprise cells from placental perfusate that are $CD34^-$, $OCT\text{-}4^+$ and $SSEA3^-$.

The claims as amended are not obvious over Pykett, Fasouliotis and Hwang. Neither Pykett nor Fasouliotis teach a cytotherapeutic unit comprising cells isolated from placental perfusate that are $CD34^-$, $OCT\text{-}4^+$ and $SSEA3^-$. Hwang does not cure this defect in Pykett and Fasouliotis, because, as discussed above, the pluripotent cells of Hwang are disclosed to be $CD34^-$, $OCT\text{-}4^+$ and $SSEA3^+$. As such, the combination of Pykett, Fasouliotis and Hwang fails to teach all limitations of the pending claims. A person of ordinary skill in the art, therefore, would not be motivated to combine these references to produce the claimed cytotherapeutic units, and would have no reasonable expectation in doing so.

For the above reasons, Applicant respectfully requests withdrawal of this rejection of the claims.

CONCLUSION

Applicant respectfully requests that the present remarks be made of record in the file history of the present application. An early allowance of the application is earnestly requested. The Examiner is invited to contact the undersigned with any questions concerning the application.

Respectfully submitted,

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